FDA Update

CLIAC Meeting

November 1, 2017

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Chemist, Division of Program Operations and Management

Office of In Vitro Diagnostics and Radiological Health (OIR)

Center for Devices and Radiological Health (CDRH)

Overview

- Organizational Changes
- Implementation of Recent Legislation Affecting the CLIA Waiver Program
  - 21st Century Cures
  - FDARA and MDUFA IV
- Semantic Interoperability Updates
- Recent Authorizations
- Upcoming Guidances, Meetings, & Workshops

Alberto Gutierrez, PhD

Retired September 2017
after 25 years of service at FDA

genomeweb

Business & Policy Technology Researc

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Gutierrez Leaving FDA After Leading Dx Regulatory Efforts During Precision Medicine Revolution

Aug 29, 2017 | Turna Ray

This article has been updated to correct Don St. Pierre's title. He is currently deputy director in the Office of In Vitro Diagnostics and Radiological Health, not associate director.

NEW YORK – Alberto Gutierrez, director of the US Food and Drug Administration's Office of In Vitro Diagnostics and Radiological Health, is leaving the agency after 25 years of public service.

Gutierrez joined the agency in 1992 as a researcher at the FDA's Center for Biologics Evaluation and Research working on methods of determining the purity and structure of vaccine components, and eventually became director of OIVD within FDA's device center in 2009. He will retire from the FDA at the end of September to explore other opportunities in the healthcare sector, but hasn't yet decided what his next steps will be.

Alberto Gutierrez; credit; Michael Ermarth, FDA

https://www.genomeweb.com/molecular-diagnostics/gutierrez-leaving-fda-after-leading-dx-regulatory-efforts-during-precision

Office of In Vitro Diagnostics and Radiological Health (OIR)

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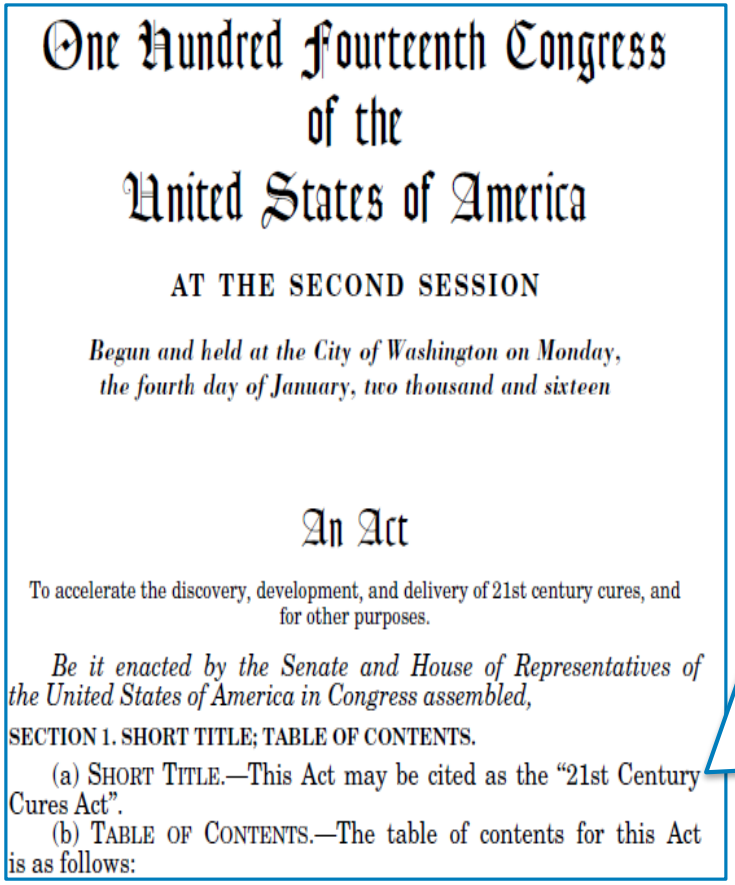
21st Century Cures



One Hundred Fourteenth Congress
of the
United States of America

AT THE SECOND SESSION

Begun and held at the City of Washington on Monday, the fourth day of January, two thousand and sixteen

An Act

To accelerate the discovery, development, and delivery of 21st century cures, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "21st Century Cures Act".

(b) TABLE OF CONTENTS.—The table of contents for this Act is as follows:

1. § 3051: Breakthrough devices
2. § 3052: Humanitarian device exemption
3. § 3053: Recognition of standards
4. § 3054: Certain class I and class II devices
5. § 3055: Classification panels
6. § 3056: Institutional review board flexibility
7. § 3057: CLIA waiver improvements
8. § 3058: Least burdensome device review
9. § 3059: Cleaning instructions and validation data
10. § 3060: Clarifying medical software regulation

21st Century Cures Requires a Draft Update to Sec V of the CLIA Waiver Guidance by Dec. 13, 2017

Sec. 3057, CLIA Waiver Improvements, requires FDA to publish a draft that:

- (1) revises "Section V. Demonstrating Insignificant Risk of an Erroneous Result – Accuracy" of the guidance entitled "Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices" and dated January 30, 2008; and

- (2) includes the appropriate use of comparable performance between a waived user and a moderately complex laboratory user to demonstrate accuracy.

FDA Reauthorization Act

One Hundred Fifteenth Congress
of the
United States of America

AT THE FIRST SESSION

Begun and held at the City of Washington on Tuesday, the third day of January, two thousand and seventeen

An Act

To amend the Federal Food, Drug, and Cosmetic Act to revise and extend the user-fee programs for prescription drugs, medical devices, generic drugs, and biosimilar biological products, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "FDA Reauthorization Act of 2017".

SEC. 2. TABLE OF CONTENTS.

The table of contents for this Act is as follows:

MDUFA PERFORMANCE GOALS AND PROCEDURES, FISCAL YEARS 2018 THROUGH 2022

General

The performance goals and procedures agreed to by the Center for Devices and Radiological Health (CDRH) and the Center for Biologics Evaluation and Research (CBER) of the United States Food and Drug Administration ("FDA" or "the Agency") for the medical device user fee program in the Medical Device User Fee Amendments of 2017, are summarized below.

FDA and the industry are committed to protecting and promoting public health by providing timely access to safe and effective medical devices. Nothing in this letter precludes the Agency from protecting the public health by exercising its authority to provide a reasonable assurance of the safety and effectiveness of medical devices. Both FDA and the industry are committed to the spirit and intent of the goals described in this letter.

I. Shared Outcome Goals

The program and initiatives outlined in this document are predicated on significant interaction between the Agency and applicants. FDA and representatives of the industry agree that the process improvements outlined in this letter, when implemented by all parties as intended, should reduce the average Total Time to Decision for PMA applications and 510(k) submissions, provided that the total funding of the device review program adheres to the assumptions underlying this agreement. FDA and applicants share the responsibility for achieving this objective of reducing the average Total Time to Decision, while maintaining standards for safety and effectiveness. Success of this program will require the cooperation and dedicated efforts of FDA and applicants to reduce their respective portions of the total time to decision.

FDA will be reporting total time performance quarterly as described in Section VI. FDA and industry will participate in the independent assessment of progress toward this outcome, as described in Section V below. As appropriate, key findings and recommendations from this assessment will be implemented by FDA.

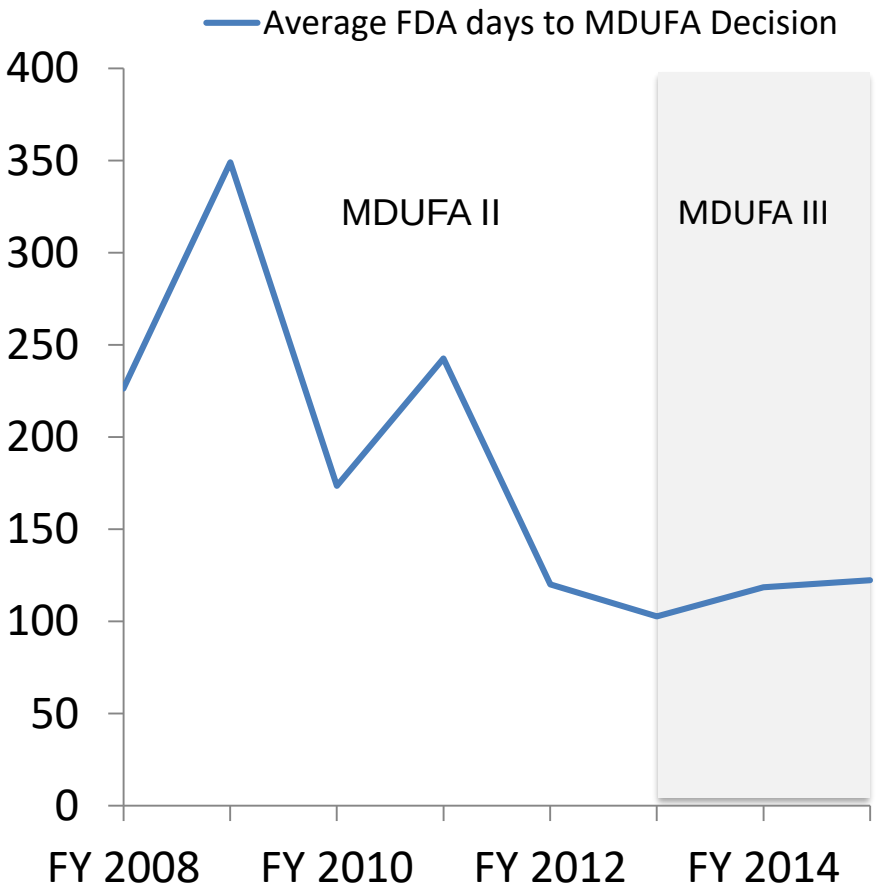
A. PMA

FDA will report on an annual basis the average Total Time to Decision as defined in Section VII.H for the three most recent closed receipt cohorts.

CLIA Waiver Program Improvements

- MDUFA IV Performance Goals
  - Shorter times to decision
  - Missed MDUFA decision process
- Central Program Oversight
- Additional Guidance (coming soon)
  - Draft update to Section V. of CLIA Waiver by Application Guidance
  - Draft guidance on Dual 510(k) and CLIA Waiver by Application
- CLIA Waiver Decision Summaries Pilot

Average Review Times for CLIA Waivers Have Dropped Dramatically Since 2008



- Process improvements and performance goals in MDUFA III lead to more efficient CW reviews
- Additional CW resources provided by MDUFA IV will allow FDA to reach faster performance goals and make additional CW program improvements

CDRH Transparency
Overview of CDRH Transparency
CDRH Transparency: Total Product Life Cycle (TPLC)
CDRH Transparency: Premarket Submissions
CDRH Transparency: Postmarket Performance and Safety
CDRH Transparency: Compliance & Enforcement
CDRH Transparency: Science & Research
CDRH Transparency: Educational Resources
CDRH Performance Data
CDRH Transparency Website Feedback Summary

CLIA Waiver by Application Decision Summaries

Under the Clinical Laboratory Improvement Amendments (CLIA), the FDA categorizes in vitro diagnostic (IVD) tests by their degree of complexity: waived, moderate complexity, and high complexity.

Tests that are waived by regulation under 42 CFR 493.15(c), or cleared or approved for home use or for over-the-counter use, are automatically categorized as waived following clearance or approval. Otherwise, following clearance or approval, tests may be categorized either as moderate or high complexity according to the CLIA categorization criteria listed in 42 CFR 493.17.

A manufacturer of a test categorized as moderate complexity may request categorization of the test as waived through a CLIA Waiver by Application (CW) submission to FDA. In a CW, the manufacturer provides evidence to FDA that a test meets the CLIA statutory criteria for waiver, 42 U.S.C. § 263a(d)(3).

To increase transparency into FDA's decision-making processes, the FDA is piloting the release of CLIA Waiver by Application (CW) Approval Determination Decision Summaries. Each Decision Summary contains a review of the data submitted by an applicant to support the determination that a test system meets CLIA statutory criteria for waiver, and FDA's justification in approving the CW application. CLIA Waiver Decision Summaries will allow the public to learn how the FDA reviewed an applicant's data to make a CW approval determination and provide information that is useful for manufacturers preparing future CW applications. For example, Decision Summaries allow manufacturers to see what types of flex studies and clinical studies other applicants conducted so that they may conduct similar studies.

During this pilot, CW Decision Summaries will be posted below as they become available. For questions or comments about the CW Decision Summary Pilot, please contact CLIA@fda.hhs.gov.

Test System Name	Document Number	FDA Review Decision Summary	Effective Date (DD/MM/YYYY)
Quidel Sofia 2 (Sofia RSV FIA)	CW170001	CW170001.pdf Decision Summary	06/28/2017
Quidel Sofia 2 (Sofia Influenza A+B FIA)	CW160016	CW160016.pdf Decision Summary	05/30/2017

https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm578178.htm

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Lab Data Interoperability/RWE/TPLC

Systemic Harmonization & Interoperability Enhancement for Lab Data (SHIELD) :

Improve decision support, real-time epidemiology, healthcare cost savings, access Real-World Evidence (RWE) throughout the Total Product Life Cycle (TPLC) and more…

OIR is currently:

- Engaging in cross-center multi-stakeholder consensus efforts to aid the adoption of semantic interoperability and structured data format standards into lab workflow.
  - Unambiguous step-by-step manual defining how to map LOINC to IVD devices
  - Clinical IVD Semantic Interoperability Meeting – Value Sets *(Jan. 22-23, 2018)*
  - 2 PCORTF lab data interoperability grants for Acute Kidney Injury (AKI) and opioid data
- Providing guidance on how to leverage RWE and safely disseminate data harmonization information to increase access to meaningful RWE.

Critical Involved Stakeholders:

FDA (CDRH, CDER, CBER), CDC, NIH, ONC, CMS, IVD Manufacturers, EHR Vendors, Laboratories, CAP, Standards Developers, Academia

Questions/Comments? *Michael.Waters@FDA.hhs.gov*

Efforts Driving SHIELD Development

(Systemic Harmonization & Interoperability Enhancement for Lab Data)

2013

FDA engaged CDISC to advocate for LOINC inclusion in IVDs device

2014

- Assembly of multi-stakeholder consensus forum for lab data semantic interoperability
- UDI for Class III devices

2015

- FDA/CDC/NLM Lab Data Interoperability Wkshp
- Whitepaper for Harmonization of lab data
- Recognized Standards: *LOINC, SNOMED-CT*
- Draft of LIVD

2016

- Draft Guidances: *RWE, Interoperability, NGS Database*
- FDA/CDC/NLM/ONC/CMS Lab Data Interoperability Wkshp
- LIVD Launch
- UDI for Class II Devices

- Final Guidances: *RWE, Interoperability, NGS Database*
- Draft of HL7/FHIR implementation guide
- Engage Lab US Realm
- Submit PCORTF grants

CDISC: Clinical Data Interchange Standards Consortium
LOINC: Logical Observations Identifiers Names and Codes
SNOMED: Systematized Nomenclature of Medicine-Clin Terms
LIVD: IVD Structured Data Format
CDC: Centers for Disease Control
NLM: Nat'l Library of Medicine
ONC: Office of the Nat'l Coordinator
CMS: Center for Medicare and Medicaid Services
NGS: Next Generation Sequencing
HL7: Health-Level 7
FHIR: Fast Healthcare Interchange Resource
PCORTF: Patient-Centered Outcome Research Trust Fund

SHIELD – Infrastructure

Function	*Candidate Coding*	*Elements (partial list)*	*Transmission Format*
Describe IVD device/method type	LOINC (Logical Observations Identifiers Names and Codes)	Component Property Time System Scale Method	Structured Data Format -LIVD
Describe IVD device/method result	SNOMED-CT (Systematized Nomenclature of Medicine – Clinical Terms)	Detected Not Detected Inconclusive Test Not Completed	Structured Data Format –LIVD II
	UCUM (Unified Code for Units of Measure)	Units of Measures (e.g. grams, etc.)	Structured Data Format –LIVD II
Unique Device Identification	UDI (FDA Unique Device Identification System)	Device Identifier Elements of UDI	Structured Data Format -LIVD

Associated data populated into Laboratory Information Systems (LISs) can be queried. Fast Healthcare Interchange Resource (FHIR) implementation guide is near completion.

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CLIA Waivers by Application

- Alere BinaxNOW Influenza A & B Card 2 with Reader
- Quidel Sofia 2 (Sofia RSV FIA)
- Quidel Sofia 2 (Sofia Influenza A+B FIA)
- Acon Labs Mission U120 Urine Chemistry Test System (Microalbumin/Creatinine)

De Novo Classifications

- ID-FISH Plasmodium Genus Test Kit, ID-FISH Plasmodium falciparum and P. vivax Combo Test Kit
- Philips IntelliSite Pathology Solution (PIPS)
- 23andMe Personal Genome Service (PGS) Genetic Health Risk Test
- QuantX Radiological computer-assisted diagnostic (CADx) software for lesions suspicious for cancer
- ClearLLab Reagents (T1, T2, B1, B2, M)

PMAs

- Freestyle Libre Flash Glucose Monitoring System
- PD-L1 IHC 22C3 pharmDx
- ZEUS ELISA Parvovirus B19 IgM Test System
- ZEUS ELISA Parvovirus B19 IgG Test System
- t:slim X2 Insulin Pump with Dexcom G5 Mobile CGM
- Abbott RealTime IDH2 (somatic gene mutation detection system)
- Praxis Extended RAS Panel (NGS oncology panel, somatic or germline variant detection system)
- Oncomine Dx Target Test (NGS oncology panel, somatic or germline variant detection system)

Emergency Use Authorizations

- Chembio Diagnostic System, Inc. - DPP Zika IgM Assay System
- Siemens Healthcare Diagnostics Inc. - ADVIA Centaur Zika Test
- Thermo Fisher Scientific - TaqPath Zika Virus Kit (ZIKV)
- Columbia University - CII-ArboViroPlex rRT-PCR Assay

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OIR FY 2018 Guidance Priorities

- Draft Updates to **Section V of CLIA Waiver** Guidance
- Draft Guidance on **Dual 510(k) and CLIA Waiver** by Applications
- (new) Draft Guidance on **510(k) Third Party Premarket Review** Program
- (new) Draft Guidance on **Replacement Reagents** for Technologically Similar Instruments Policy for In Vitro Diagnostic Devices
- Draft Guidance on **Investigational IVD Devices** Used in Clinical Investigations of Therapeutic Products

- Final Guidance on Considerations for **Design, Development, and Analytical Validation of Next Generation Sequencing (NGS)-Based In Vitro Diagnostics (IVDs)** Used to Aid in the Diagnosis of Suspected Germline Diseases
- Final Guidance on Use of Public Human Genetic Variant **Databases to Support Clinical Validity** for Genetic and Genomic-Based In Vitro Diagnostics
- Final Guidance on Principles for **Codevelopment** of an In Vitro Companion Diagnostic Device with a Therapeutic Product

Public Meetings & Workshops

- Nov 28, 2017: Cardiac Troponin Public Workshop
- Jan 11, 2018: Self-Collection Devices for Pap Test
- Jan 29, 2018: Variant Classification and Interpretation in Precision Oncology

Thank you

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FDA
U.S. FOOD & DRUG
ADMINISTRATION